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EXAMINER	
JAGOE, DONNA A	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/577,760	LULLA ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,31-42,61,80-82,86 and 87* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17,31-42,61,80-82,86 and 87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/18/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-17, 31-42, 61, 80-82, 86 and 87 are presented for examination.

Claim Objections

Claim 4 is objected to because of the following informalities: the claim appears to be amended to depend from claim 3, however, presently the claim recites "A pharmaceutically acceptable oral formulation according to **4 claim 3**, wherein said 5-HT-receptor agonist is sumatriptan succinate. Appropriate correction is required.

Specification

The use of the trademark Opaglos 6000® has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 U.S.C. § 112, (First Paragraph)

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and

use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-17, 31-42, 61, 80-82, 86 and 87 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a 5-HT-receptor agonist, or a pharmaceutically acceptable salt, does not reasonably provide enablement for *solvates or derivatives thereof*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention(s) commensurate in scope with these claims. *Solvates and derivatives*, as recited in claims 1-3, 61 and 86 have not been adequately enabled in the specification to allow any person having ordinary skill in the art, at the time this invention was made, to make and use a 5-HT-receptor agonist, or a pharmaceutically acceptable salt and *solvates and derivatives* thereof.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is *undue*. These factors include, but are not limited to: (a) breadth of the claims; (b) nature of the invention; (c) state of the prior art; (d) level of one of ordinary skill in the art; (e) level of predictability in the art; (f) amount of direction provided by the inventor; (g) existence of working examples; and (h) quantity of experimentation needed to make or use the invention based on the content of the disclosure. (See *Ex parte Forman* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988).

The above factors, regarding the present invention, are summarized as follows:

(a) *Breadth of the claims* - the breadth of the claims includes all 5HT receptor agonists, as well as the myriad of potential solvates and derivatives, formulated from these 5-HT receptor agonists;

(b) *Nature of the invention* - the nature of the invention is a pharmaceutical compositions comprising an oral formulation of a 5-HT receptor agonist and its *solvates and derivatives*;

(c) *State of the prior art – Advanced Drug Delivery Reviews 48 (2001) 3-26* teach that Crystalline solids can exist in the form of polymorphs, solvates or hydrates. Phase transitions such as polymorph interconversion, desolvation of solvate, formation of hydrate and conversion of crystalline to amorphous form may occur during various pharmaceutical processes, which may alter the dissolution rate and transport characteristics of the drug (abstract).

(d) *Level of one of ordinary skill in the art* - the artisans synthesizing a solvate or derivative of a 5-HT receptor agonist would be a synthetic chemist possessing a commensurate degree level and/or skill in the art, as well as several years of professional experience;

(e) *Level of predictability in the art* - Synthetic organic chemistry is quite unpredictable (*In re Marzocchi and Horton* 169 USPQ at 367 ¶ 3). The following excerpt is taken from Vippagunta, et al. with respect to solvates and hydrates (Vippagunta, et al. *Advanced Drug Delivery Reviews*, 48, **2001**, p. 18):

> *Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated into the crystal lattice of a compound is complex and difficult. Each solid compound responds uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for a series of related compounds. Certain molecular shapes and features favor the formation of crystals without solvent; these compounds tend to be stabilized by efficient packing of molecules in the crystal lattice, whereas other crystal forms are more stable in the presence of water and/or solvents. There may be too many possibilities so that no computer programs are currently available for predicting the crystal structures of hydrates and solvates.*

(f) *Amount of direction provided by the inventor* - the application is negligent regarding direction with respect to making and using solvates and derivatives of 5-HT receptor agonists;

(g) *Existence of working examples* - 5-HT receptor agonists comprise a narrow subgenus, for which applicant has provided sufficient guidance to make and

use; however, the disclosure is insufficient to allow extrapolation of the limited examples to enable the scope of the myriad of instantly claimed potential solvates and derivatives. The specification lacks working examples of solvates or derivatives of any of the 5-HT agonists.

Within the specification, "specific operative embodiments or examples of the invention must be set forth. Examples and description should be of sufficient scope as to justify the scope of the claims. *Markush* claims must be provided with support in the disclosure for each member of the *Markush* group. Where the constitution and formula of a chemical compound is stated only as a probability or speculation, the disclosure is not sufficient to support claims identifying the compound by such composition or formula." See MPEP § 608.01(p).

(h) *Quantity of experimentation needed to make or use the invention based on the content of the disclosure* - predicting whether a recited compound is in fact one that produces a desired physiological effect at a therapeutic concentration and with useful kinetics, is filled with experimental uncertainty, and without proper guidance, would involve a substantial amount of experimentation. Vippagunta et al. recites that when crystal structures can be calculated with certainty, it will be possible to predict the various polymorphs of a compound and this information could be used to guide experimental studies, but this goal may be difficult to achieve owing to the complex molecular structures of new organic molecules and the Presence of several molecules in each asymmetric unit (page 23, column 2).

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

The determination that *undue experimentation* would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. These factual considerations are discussed comprehensively in MPEP § 2164.08 (scope or breadth of the claims), §

2164.05(a) (nature of the invention and state of the prior art), § 2164.05(b) (level of one of ordinary skill), § 2164.03 (level of predictability in the art and amount of direction provided by the inventor), § 2164.02 (the existence of working examples) and § 2164.06 (quantity of experimentation needed to make or use the invention based on the content of the disclosure).

Based on a preponderance of the evidence presented herein, the conclusion that applicant is insufficiently enabled for making and using solvates and derivatives of 5-HT receptor agonists is clearly justified.

Claim Rejections - 35 USC § 112 (second paragraph)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5-17, 31 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 recites "A pharmaceutically acceptable oral formulation according to any of claim 1. It is unclear what is meant by the words "any of".

Claim 5 recites that the pharmaceutically acceptable oral formulation is substantially free of degradation products associated with exposure of a 5-HT receptor agonist to "ambient moisture". Since the "**ambient moisture**" is not defined in the specification, the meaning is unclear. Turning to the dictionary, the meaning of "ambient" merely means surrounding a subject. Dependent upon where you live and

under what conditions, ambient moisture can vary greatly. The definition from http://encyclopedia.thefreedictionary.com/Ambient+moisture is: the presence of moisture of the surroundings. "Ambient moisture" is a term that may be applied to the outdoors or to any place. Even once a context has been specified, "ambient moisture" may refer to no particular moisture humidity level. The ambient moisture of a place may vary in time as well as space. The temperature at a certain lattitude and longitude in the Sahara Desert will depend on whether it is night or day, windy or still and the location of the hygrometer. These variations and gradations may affect an experiment that extends over a large space or takes place over a long time. The MPEP, 2111.01 [R-2] states that the words of a claim must be given their "plain meaning" unless they are defined in the specification". During examination, the claims must be interpreted as broadly as their terms reasonably allow. In re American Academy of Science Tech Center, F.3d, 2004 WL 1067528 (Fed. Cir. May 13, 2004)(The USPTO uses a different standard for construing claims than that used by district courts; during examination theUSPTO must give claims their broadest reasonable interpretation.). This means that the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989); Chef America, Inc. v. Lamb-Weston, Inc., 358 F.3d 1371, 1372, 69 USPQ2d 1857 (Fed. Cir. 2004) (Ordinary, simple English words whose meaning is clear and unquestionable, absent any indication that their use in a particular context changes their meaning, are construed to mean exactly what they say. Thus, "heating the resulting batter-coated dough to a temperature in the range of about 400° F to 850° F" required

heating the dough, rather than the air inside an oven, to the specified temperature.). It is only when the specification provides definitions for terms appearing in the claims that the specification can be used in interpreting claim language. In re Vogel, 422 F.2d 438, 441, 164 USPQ 619, 622 (CCPA 1970). Therefore, since there is no definition in the instant specification of what is meant by the term "ambient moisture", then the meaning from the dictionary is applied,which is "no particular moisture level".

Regarding claims 6-17 that recite the term (EC) (as in 40EC or 25EC), it is customary that the full name of the abbreviation be recited the first time the abbreviation is used in the claims. The meaning of every term used in a claim should be apparent from the prior art or from the specification and drawings at the time the application is filed. Applicants need not confine themselves to the terminology used in the prior art, but are required to make clear and precise the terms that are used to define the invention whereby the metes and bounds of the claimed invention can be ascertained. During patent examination, the pending claims must be given the broadest reasonable interpretation consistent with the specification. In re Morris, 127 F.3d 1048, 1054, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997); In re Prater, 415 F.2d 1393, 162 USPQ 541 (CCPA 1969).

Claims 31and 32 contain the trademark/trade name Opaglos 6000®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used

properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a proprietary blend of ethanol, shellac, beeswax and yellow carnuba wax, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, and 31-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Patel et al. U.S. 2003/0180352 A1.

Patel et al. teach a formulation comprising 5-HT receptor agonists such as sumatriptan, eletriptan, frovatriptan, naratriptan, rizatriptan and zolmitriptan (paragraphs 46, 60, 106-107, 447, and 448) for oral use (paragraph 272) comprising a core material (paragraphs 316, 350, 360 and 390) that is substantially water resistant (hydrophobic, paragraph 104) comprising waxes such as carnauba wax, shellac, spermaceti, natural and synthetic waxes (inclusive of beeswax [natural] and Opaglos 6000® [synthetic], paragraph 259) and a moisture barrier coating (paragraph 47).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-17, 31-42, 61, 80-82, 86 and 87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patel et al. U.S. Patent Application Publication No.

2003/0180352 A1 and Oxford U.S. Patent No. 5,037,845 and in view of Remington's Pharmaceutical Sciences, 1975 (V)

Patel et al. teach a formulation comprising 5-HT receptor agonists such as sumatriptan, eletriptan, frovatriptan, naratriptan, rizatriptan and zolmitriptan (paragraphs 46, 60, 106-107, 447, and 448) for oral use (paragraph 272) comprising a core material (paragraphs 316, 350, 360 and 390) that is substantially water resistant (hydrophobic, paragraph 104) comprising waxes such as carnauba wax, shellac, spermaceti, natural and synthetic waxes (inclusive of beeswax [natural] and Opaglos 6000® [synthetic], paragraph 259).

Patel et al. does not teach sumatriptan succinate.

Oxford teaches succinate is the preferred salt for the formulation of sumatriptan (column 3, lines 10-11) for oral administration (paragraph 13, line 61 to paragraph 14, line 47) for treatment of migraine headache (column 3, lines 12-18).

Patel et al. does not teach a product that is "free of degradation products with exposure of a 5-HT receptor agonist to ambient moisture", however, Patel et al. teach that spray congealing method is particularly suitable for moisture sensitive substances, since non-aqueous compositions can be utilized. It is completed before the product comes in contact with any equipment surface (paragraph 333). Hence since the composition of Patel is a core with a waxy coat the coat is employed with particular consideration to moisture sensitive substances, it meets the claim in that there are no degradation products therein. As noted in *In re Best* (195 USPQ 430 (CCPA 1977)), and *In re Fitzgerald* (205 USPQ 594 (CCPA 1980)), the mere recitation of newly-discovered

function or property, inherently possessed by things in prior art, does not cause claims drawn to those things to distinguish over prior art. In such a situation, the burden is shifted to the applicant to prove that subject matter shown to be in prior art does not possess characteristic relied on where it has reason to believe that functional limitation asserted to be critical for establishing novelty in claimed subject matter may be inherent characteristic of prior art; whether rejection is based on "inherency" under 35 U.S.C. 102, on "prima facie obviousness" under 35 U.S.C. 103, jointly or alternatively, burden of proof is same. Although the storage conditions are not disclosed in the prior art, Patel et al. teach an improved storage stability of the active ingredient (paragraph 284). Further, Remington's Pharmaceutical Sciences teach that one could extrapolate the results of an extreme storage conditions test using the Arrhenius equation to calculate longer storage stability based on normal conditions, i.e. room temperature and normal humidity (see figure 19-2 page 279 and pages 283-284). The examiner cannot calculate the storage stability Patel et al. because the specifics of the storage conditions test are not provided. However, it would have been obvious to one of ordinary skill in the art to calculate the storage stability of the composition motivated by the teaching of Remington's Pharmaceutical Sciences that the storage stability is predictable based on a linear Arrhenius plot. When the general conditions are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In this case, it would have been obvious to one of ordinary skill in the art to predict the storage stability under various conditions motivated by the teaching of Patel et al. who teach substantially water resistant (hydrophobic, paragraph 104) 5-HT receptor agonist

composition comprising, for example, sumatriptan, and waxes such as carnauba wax, shellac, spermaceti, natural and synthetic waxes (inclusive of beeswax [natural] and Opaglos 6000® [synthetic], paragraph 259) and a moisture barrier coating (paragraph 47) and the teachings of Remington's Pharmaceutical Sciences who teach that storage stability is predictable based on a linear Arrhenius plot. Regarding instant claims 35-38, drawn to core materials, Patel et al. teach sumatriptan, mannitol (paragraph 220, 230, 247 and 248), calcium carbonate, dibasic calcium phosphate, microcrystalline cellulose, croscarmellose, sodium, and magnesium stearate (paragraph 248). The specific weight ratio of sumatriptan to excipients such as, mannitol, dibasic calcium phosphate, microcrystalline cellulose, croscarmellose and magnesium stearate is not specifically disclosed, However, Patel et al. teach that the ratio of excipients to active ingredient, e.g. sumatriptan is about 5-95 wt % and preferably 20-80 wt% based on the total weight of the formulation which overlaps with the instantly claimed amount of active agent of 20-55% sumatriptan succinate. "[A] prior art reference that discloses a range encompassing a somewhat narrower claimed range is sufficient to establish a prima facie case of obviousness." *In re Peterson*, 315 F.3d 1325, 1330, 65 USPQ2d 1379, 1382-83 (Fed. Cir. 2003). See also *In re Harris*, 409 F.3d 1339, 74 USPQ2d 1951 (Fed. Cir. 2005). In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Regarding claims 86 and 87 drawn to the process of making the oral formulation, Patel et al. teach the process of making an oral composition comprising a water resistant coated core (see supra) and further teach methods of wet granulation and compression techniques (paragraphs 272).

Thus the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Accordingly, for the above reasons, the claims are deemed properly rejected and none are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Donna Jagoe /D. J./
Examiner
Art Unit 1614

May 22, 2009

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614